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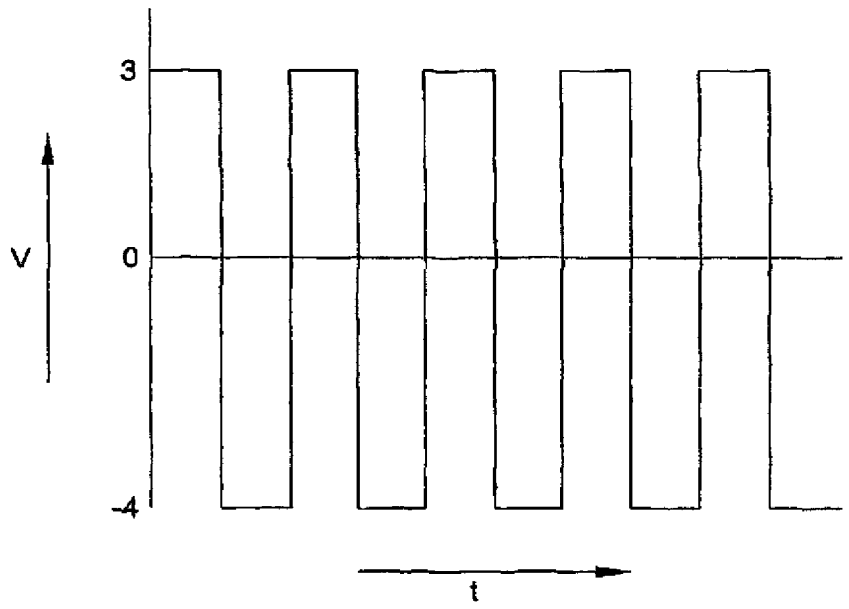

(57) Abstract: Apparatus and method for controlling electrophoresis of a system included in a channel or of multiple electrophoretic systems arranged in a matrix. The control takes place by means of a rectified voltage and alternating voltages applied across each electrophoretic system. In the multiple electrophoretic systems, electrodes are connected with each other in each row and in each column.

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APPARATUS AND METHOD FOR CONTROLLING ELECTROPHORESIS

The invention relates to a device for controlling electrophoresis, which device is provided with an electrophoretic system included in a channel, comprising a multiplicity of charged particles included in a medium, which device is further provided with control means arranged to apply a rectified voltage across at least a part of the electrophoretic system.

Such a device is known per se.

A display may, for instance, be provided with one or several of such devices. In such an electrophoretic system included in a display, the charged particles often comprise particles that are provided with a color different from the color of the medium. By means of the rectified voltage across at least a part of the electrophoretic system, the charged particles can be moved from, for instance, an actuation side to a view side so as to control the visual appearance, and in particular the color, of the view side. In such a case, the display often comprises multiple channels each provided with an electrophoretic system across which a rectified voltage can be applied. By separate drive of each individual device, images can be generated on the display.

However, an electrophoretic system as referred to in this application may also be a biological system in which the charged particles comprise a biological substance, such as, for instance, a fragment of a DNA structure or a protein. In such cases, the medium comprises, for instance, a microporous gel.

The control means often comprise electrodes to be able to apply the rectified voltage across at least a part of the electrophoretic system. When an electrode is placed at each end of the channel, the time t that the particles require to get from one electrode to the other electrode under the influence of the rectified voltage equals, by a simple approximation,

$$t \approx \frac{6\pi d^2 \eta}{V \varepsilon \xi}$$

wherein d equals the distance between the electrodes; η is the viscosity of the medium; ε is the dielectric constant of the medium; V is the potential difference between the electrodes; and ξ is the zeta potential of the particles. The system is often optimized to limit the time t to a minimum. In the example in which the device is used as a display element, a short time t means that given a proper control the display element can rapidly change in color. On an electrophoretic display comprising a multiplicity of such display elements, the images can rapidly succeed each other, given a suitable control for that purpose. To that end, in many cases, the distance d between the electrodes is minimized to limit the time t.

A problem is that sometimes the other parameters cannot be changed because, for instance, the particles and the medium are given. For instance in an application where a purpose of the electrophoresis is to separate charged DNA fragments from a biological substance, the particles and the medium can hardly, if at all, be optimized to shorten the time t. Also, from practical considerations the potential difference V cannot always be increased without introducing other drawbacks and/or problems. One of these problems is, for instance, the strong coagulation of the particles near an electrode to which the particles are attracted under the influence of a high rectified voltage.

The formula, as stated, is a simple approximation. For instance, according to the formula, the response of the particles in terms of speed would be constant if all parameters are constant. However, the speed of the particles is of course far from constant when the particles are set in motion from a condition of rest under the influence of a voltage applied across the medium. Nor do the particles move at a uniform speed once they have arrived at an electrode to which they are attracted. In general, a response of the particles to a voltage applied across the medium is very slow and/or very

low. In this case, response is understood to mean the attainment of a particular extent of electrophoresis.

This extent of electrophoresis may be expressed, for instance, in a number of particles having traveled a defined distance within the medium after a defined time. In an electrophoretic system functioning as display element, the extent of electrophoresis may be determined, for instance, on the basis of the attainment of a color intensity of the system on a view side of the display element within a specific time.

It is an object of the invention to provide a device with which the response of the particles can be improved in comparison with a response of the particles in known devices.

The stated object is achieved with a device according to the invention, which is characterized in that the control means are further arranged to superpose on the rectified voltage an alternating voltage generated in balance around a zero voltage.

Surprisingly, this has the effect that the response of the particles is better in comparison with the case where only the rectified voltage is applied across the electrophoretic system. This can mean, for instance, that the electrophoresis can be carried out more rapidly. In a display element, this implies that the visual appearance of an electrophoretic system included in such a device can for instance be controlled more rapidly than in a known device. Moreover, an undesired coagulation of particles can be prevented. In the example of the separation of DNA particles from a biological substance, this implies that the separation process can proceed more rapidly.

A better response, however, need not mean that the speed of the particles is higher, but can also mean that the amount of particles moved to a desired position in the medium is higher than the amount of particles moved to a desired position within a comparable time.

In a further embodiment, it holds that the channel is provided at a first channel end and at a second channel end with, respectively, a first electrode and a second electrode, the control means being arranged to apply to the first electrode the rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage. This provides the advantage that a voltage, such as, for instance, a zero voltage, can be imposed on the second electrode in a simple manner. However, a voltage imposed on the second electrode may also be a voltage aimed at changing the effect of the voltage imposed on the first electrode. This increases the possibilities of simply controlling electrophoresis in an electrophoretic system in a desired manner.

Thus, in a special embodiment, it may hold that the control means are further arranged to impose on the second electrode a second alternating voltage generated in balance around a zero voltage. Surprisingly, it has turned out that when applying across the electrophoretic system a voltage comprising a rectified voltage having superposed thereon an alternating voltage having a relatively high amplitude, the response of the particles is still better, compared with the case where a rectified voltage having superposed thereon an alternating voltage having a relatively low amplitude is applied across the electrophoretic system. Accordingly, this special embodiment provides the advantage that the effect of the rectified voltage with the first alternating voltage superposed thereon as imposed on the first electrode can, if desired, be enhanced. This does not require the amplitude of the first alternating voltage to be increased, but instead only the correct second alternating voltage must be imposed on the second electrode. It has turned out that under the influence of the rectified voltage having superposed thereon the alternating voltage of a relatively high amplitude, generated in balance around a zero voltage, the particles move better through the medium in comparison with particles subjected to a

rectified voltage having superposed thereon an alternating voltage of a relatively low amplitude, generated in balance around a zero voltage.

In the example of the electrophoretic display, this may imply that the images, if desired, can change even more rapidly. Also, the effect of the measure may imply that more particles can contribute to a color, so that parameters like brightness and contrast can be favorably changed.

When the electrophoresis is aimed at the separation within the system of, for instance, charged DNA fragments and the medium, the rate and/or the yield of the separation can be increased by means of the alternating voltage imposed on the second electrode. In methods for isolating DNA, this can be a major advantage.

In an even more special embodiment, it holds that the control means are further arranged to present the second alternating voltage in a phase which is substantially opposite to the phase of the first alternating voltage if according to a predetermined program the charged particles are to change position in the electrophoretic system, and it further holds that the control means are arranged to present the second alternating voltage in a phase which is substantially equal to the phase of the first alternating voltage if according to the predetermined program the charged particles in the electrophoretic system are to substantially maintain an assumed position in the electrophoretic system.

This provides the advantage that, in addition to enhancing the effect of the rectified voltage with the first alternating voltage superposed thereon as imposed on the first electrode, it is also possible to weaken this effect, if desired. The enhancement or weakening is controllable with the phase difference to be applied between the first alternating voltage and the second alternating voltage. Thus, the device can be designed in a simple manner and yet provide many possibilities of controlling the electrophoresis to a desired extent, since, instead of adjusting the height of the amplitude of the first alternating voltage to obtain an enhancement or a weakening, only the

phase of the second alternating voltage with respect to the phase of the first alternating voltage needs to be adapted.

Thus, an electrophoresis can, for instance, be carried out completely in an accelerated manner. Within the meaning of this application, a complete electrophoresis includes the charged particles having traveled the maximum bridgeable distance between the electrodes and/or, for instance, all charged particles having traveled the distance between the electrodes. In this case, the phase of the second alternating voltage must be substantially opposite to the phase of the first alternating voltage. In the example of the electrophoretic display, this implies that there is a possibility of increasing to an ample extent the rate at which the images can be alternated. In fact, the movement of the particles can take place very rapidly by effectively obtaining an alternating voltage from a high amplitude. The time t consequently required for a complete electrophoresis can be very short. When the phase of the second alternating voltage is substantially equal to the phase of the first alternating voltage, the effect of the first alternating voltage is virtually completely undone by the second alternating voltage, and the particles will only relatively slowly, and hence hardly, change position.

A very special embodiment of a device according to the invention is characterized in that the control means are arranged to maintain for a predetermined length of time the rectified voltage with the first alternating voltage superposed thereon, the control means further being arranged to cause, after a time shorter than the predetermined length of time, the second alternating voltage to make a phase jump of substantially half a wavelength to obtain a partial electrophoresis within the predetermined length of time.

This provides the advantage that, if desired, a partial electrophoresis can be controlled as a function of the time in which the second alternating voltage is imposed on the second electrode within a predetermined length of

time in a phase equal to the phase of the first alternating voltage. In this connection, a partial electrophoresis can be understood to mean that within the predetermined length of time the particles have traveled only a part of the maximum bridgeable distance between the electrodes. It could also be understood to mean that not all particles travel the maximum distance between the electrodes. A device according to this embodiment can be arranged in a very simple manner to enable a very accurate control of a desired extent of electrophoresis within a standardized length of time. Moreover, this length of time can be very short, since the standardized length of time can be the length of time required for the particles to bridge the maximum distance to be traveled at a rectified voltage with the first alternating voltage superposed thereon as imposed on the first electrode and an alternating voltage imposed on the second electrode, enhancing the effect of the first alternating voltage. Any desired extent of electrophoresis that does not correspond to a complete electrophoresis can be achieved in a simple manner within the standard length of time. For the example of the electrophoretic display built up from a multiplicity of such devices, this provides the advantage that a so-called gray shade can be provided in a display element in a rapid and simple manner. By such a gray shade is meant a shade midway between the color that the view side of the display element shows when all the particles are on the view side and the color that the view side of the display element shows when all particles are on the side remote from the view side. In that case, in a black-and-white display, it is possible to provide true gray shades. In a color display this affords a possibility of controlling brightness. Also, this embodiment offers a possibility of forming mixed colors.

An elaborated embodiment of a device according to the invention is characterized in that the electrophoretic system included in a channel is included in a matrix of mutually separated channels each provided with an electrophoretic system and each provided on a first and a second side with

respectively a first electrode and a second electrode, which matrix comprises at least two rows and at least two columns, while in each row the first electrodes are electrically connected with each other, and in each column the second electrodes are electrically connected with each other.

This embodiment provides the advantage that a desired extent of electrophoresis can be controlled in multiple electrophoretic systems with relatively simple control means. Individual first and second electrodes for each electrophoretic system included in a separate channel have thus become superfluous. Moreover, this implies that the multiple channels could, for instance, be included in a flexible foil against which flexible first electrodes and flexible second electrodes are provided, in rows on a first side of the foil and columns on a second side of the foil, respectively. This allows the manufacture of flexible electrophoretic displays.

A more practical embodiment of such a device according to the invention is characterized in that the control means are arranged to select, according to a predetermined sequence, a row for imposing on the first electrode of the selected row the rectified voltage with the first alternating voltage superposed thereon, and to control, according to the predetermined program, through imposing the second alternating voltage on each second electrode, a desired extent of electrophoresis in each electrophoretic system located in the selected row. This provides the advantage that the desired extent of electrophoresis of each individual electrophoretic system located in a row can be controlled. This is because on the first electrode, the rectified voltage with the first alternating voltage superposed thereon can be imposed, and on each second electrode the second alternating voltage can be imposed, while the phase with respect to the first alternating voltage and/or the time over which the second alternating voltage in a particular phase is applied can be different per second electrode, for instance according to a predetermined program.

Furthermore, in a further elaboration, it may hold that the control means are further arranged to impose a zero voltage on the first electrode of a row if the desired extent of electrophoresis has already been controlled in each electrophoretic system located in that row. This provides the advantage that across the electrophoretic systems of which the desired extent of electrophoresis has already been controlled, only the second alternating voltage generated around a zero voltage will be applied. This has as a result that while the particles might become involved in a back-and-forth movement, they will in effect hardly, if at all, change in position. This is because the second alternating voltage is an alternating voltage generated in balance around a zero voltage and comprises, besides the second alternating voltage, no rectified voltage component. The already controlled desired extent of electrophoresis will therefore not be undone.

In addition, this embodiment solves the alleged problem that an electrophoretic display comprising electrophoretic systems arranged in a matrix is not drivable with a so-called passive drive. In other words, it proves to be quite possible to drive electrophoretic displays with first electrodes which, on a first side of the multiple electrophoretic systems arranged in a matrix, electrically interconnect the electrophoretic systems positioned in one row, and with second electrodes which, on a second side of the multiple electrophoretic systems arranged in a matrix, electrically interconnect the electrophoretic systems positioned in one row. Heretofore, this was considered impossible because, as is often assumed, electrophoretic systems do not have a threshold voltage for getting the particles to move. In the absence of a threshold voltage, in case of a passive drive, undesired influencing of particles in a non-selected electrophoretic system cannot be precluded.

Furthermore, the control means can be arranged to impose a relatively high rectified voltage on the first electrode of a row of which in each electrophoretic system positioned in that row the desired extent of

electrophoresis is yet to be controlled. In this way, a starting position can be fixed for each electrophoretic system positioned in a row of which the desired extent of electrophoresis is yet to be controlled. The relatively high rectified voltage is preferably so high that the second alternating voltage has no influence on the particles in the electrophoretic systems across which the relatively high rectified voltage has been applied.

As stated before, for the purpose of the application of a display, the particles can be provided with a color different from a color of the medium.

At least one of the particles in the electrophoretic system can comprise a biological substance, and preferably even a fragment of DNA. One of the particles can comprise, for instance, a protein. In such a case, the medium can comprise a microporous gel. In that case, the multiple electrophoretic systems arranged in a matrix can provide a device with which, on a large scale, many different experiments can be carried out according to a predetermined program relatively fast and/or with a high yield.

The invention further relates to a method for controlling electrophoresis of an electrophoretic system which comprises a multiplicity of charged particles included in a medium.

In addition, the invention relates to a method for controlling electrophoresis in multiple electrophoretic systems arranged in a matrix.

The invention will now be explained with reference to a drawing, in which:

Fig. 1a shows a diagram of a rectified voltage and an alternating voltage generated in balance around a zero voltage for realizing a first embodiment of the invention;

Fig. 1b shows a voltage gradient obtained by superposing the voltage profiles shown in Fig. 1a;

Fig. 2a shows a voltage gradient imposed on a first electrode, according to a second embodiment;

Fig. 2b shows a voltage gradient imposed on a second electrode, according to the second embodiment;

Fig. 2c shows a voltage gradient effectively applied across an electrophoretic system according to the second embodiment;

Fig. 2d shows a schematic electrophoresis diagram of an electrophoretic system across which a voltage gradient according to Fig. 2c has been applied;

Fig. 3a shows a voltage pattern imposed on the first electrode according to an alternative second embodiment of the invention;

Fig. 3b shows a voltage gradient imposed on the second electrode according to the alternative second embodiment of the invention;

Fig. 3c shows a voltage gradient effectively applied across the electrophoretic system according to the alternative second embodiment of the invention;

Fig. 3d shows a schematic electrophoresis diagram of an electrophoretic system across which the voltage gradient of Fig. 3c has been applied;

Fig. 4a shows a voltage pattern imposed on a first electrode according to a third embodiment of the invention;

Fig. 4b shows a voltage pattern imposed on a second electrode according to the third embodiment of the invention;

Fig. 4c shows a voltage gradient effectively applied across an electrophoretic system according to the third embodiment of the invention;

Fig. 4d shows an electrophoresis diagram of an electrophoretic system across which the voltage gradient of Fig. 4c has been applied;

Fig. 5a shows a voltage gradient imposed on a first electrode according to an alternative third embodiment of the invention;

Fig. 5b shows a voltage gradient imposed on a second electrode according to the alternative third embodiment of the invention;

Fig. 5c shows a voltage gradient effectively applied across an electrophoretic system according to the alternative third embodiment of the invention;

Fig. 5d shows an electrophoresis diagram representing the electrophoresis of an electrophoretic system across which a voltage gradient according to Fig. 5c has been applied;

Fig. 6a schematically shows a fourth embodiment of a device according to the invention with a schematic representation of a method according to the invention; and

Fig. 6b shows the fourth embodiment schematically shown in Fig. 6a in a later phase in a method according to the invention.

A device for controlling electrophoresis of an electrophoretic system included in a channel is provided with control means which are arranged to apply a rectified voltage across at least a part of the electrophoretic system. Such a rectified voltage is indicated in a diagram of Fig. 1a with a dotted line. According to the invention, the control means are further arranged to superpose on the rectified voltage an alternating voltage generated in balance around a zero voltage. An example of an alternating voltage generated in balance around a zero voltage is indicated in Fig. 1a with a full line in the diagram. A multiplicity of charged particles included in a medium of the electrophoretic system is moved through the medium under the influence of the rectified voltage and the alternating voltage generated in balance around a zero voltage, as represented in Fig. 1a. In effect, the particles are thus subjected to a voltage gradient as represented in the diagram of Fig. 1b. According to this voltage pattern, the particles are, as expected, moved back and forth through the medium. As represented in this example, a voltage difference of –4 V and a voltage difference of 3 V is alternately applied over the particles. As a result, the particles will net change in position. It has turned out that a response of the particles is achieved faster upon subjecting the particles to a voltage gradient as shown

in the diagram of Fig. 1b than upon subjecting them to a rectified voltage as shown in the diagram of Fig. 1a with the dotted line. In other words, the time the particles need to bridge a distance between two electrodes can, when they are subjected to a voltage gradient as shown in the diagram of Fig. 1b, be much shorter than the time the particles need when subjected to a rectified voltage as shown with the dotted line in the diagram of Fig. 1a.

It may also be that after a particular unit of time more particles have arrived at an electrode when the particles have been subjected to a voltage gradient according to Fig. 1b, in comparison with particles subjected to a voltage gradient according to the dotted line in Fig. 1a.

According to a second embodiment of a device according to the invention, the channel with the multiplicity of charged particles included in a medium is provided, at a first channel end and at a second channel end, with a first electrode and a second electrode, respectively. The control means are further arranged to impose on the first electrode the rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage. On the first electrode, therefore, a voltage gradient as shown in Fig. 2a is imposed. The control means are further arranged to impose on the second electrode a second alternating voltage generated in balance around a zero voltage. This second alternating voltage generated around a zero voltage may correspond to a voltage gradient as shown in Fig. 2b. In effect, a voltage gradient as shown in Fig. 2c is applied across the electrophoretic system positioned between the first and the second electrode. Certainly in a short time, the particles subjected to a voltage gradient according to Fig. 2c will hardly change position in the medium. Accordingly, the electrophoresis will hardly, if at all, proceed, as shown in the electrophoresis diagram according to Fig. 2d.

It may also be, however, that on the first electrode, again a voltage gradient according to Fig. 2a, see Fig. 3a, is imposed, but that on the second electrode a second alternating voltage generated in balance around a zero

voltage is imposed, which is opposite in phase to the phase of the first alternating voltage imposed on the first electrode. In that case, the multiplicity of charged particles included in a medium of the electrophoretic system is in effect subjected to a voltage gradient as shown in Fig. 3c. With such a voltage gradient, the particles will in a relatively short time, and/or relatively many particles will in a short time, bridge a distance between the electrodes, and accordingly the electrophoresis will take place completely, as represented in the electrophoresis diagram according to Fig. 3d. It should be noted that the difference between the schematic electrophoresis diagram as shown in Fig. 2d and the electrophoresis diagram as shown in Fig. 3d is only caused by a difference in phase in the second alternating voltage imposed on the second electrode.

In a third embodiment, the control means are arranged to apply to a first electrode a rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage for a particular length of time, as shown in Fig. 4a. In this embodiment, the control means are further arranged to cause the second alternating voltage, after a time shorter than the predetermined length of time, to make a phase jump of substantially half a wavelength. In Fig. 4b, this predetermined length of time has been set to be equal to 0.5 units of time. The charged particles, included in a medium, of an electrophoretic system situated between the electrodes of this embodiment, are subjected to an undervoltage gradient as shown in Fig. 4c. At such a voltage gradient, the particles are induced from time 0 to 0.5 units of time to perform an electrophoresis. After these 0.5 units of time, the particles are hardly, if at all, subjected to a voltage anymore that results in a continuing electrophoresis. If in one unit of time a complete electrophoresis, for instance 100%, can be obtained, only 50% of the electrophoresis will take place when the charged particles are subjected to a voltage gradient as shown in Fig. 4c. This is shown in Fig. 4d. As can be derived from Fig. 4b, this partial electrophoresis has been effected

because the second alternating voltage, after a time shorter than the predetermined length of time, has made a phase jump of substantially half a wavelength. Such a partial electrophoresis can be advantageous in electrophoretic systems that are included in a display. If an electrophoretic system included in a display element comprises, for instance, black charged particles and a white medium, the display element may, in case of a complete electrophoresis, be black on a view side. In case of a partial electrophoresis, the display element may be gray.

Now, suppose again that on a first electrode of such an embodiment a rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage is imposed. See Fig. 5a. The control means may further be arranged to impose on the second electrode a second alternating voltage equal in phase to the first alternating voltage, for a length of time of, for instance, 0.25 units of time, and to impose after the 0.25 units of time a second alternating voltage opposite to the first alternating voltage. See Fig. 5b. The charged particles, included in a medium, of an electrophoretic system situated between such first and second electrodes are subjected to a voltage gradient as shown in Fig. 5c. In this case, in the first 0.25 units of time, the particles are subjected to a voltage gradient that hardly entails a change of the particles in the medium. Following the first 0.25 units of time, however, the particles are subjected to a voltage gradient that does entail a change of the position of the particles in the medium. Accordingly, in the remaining length of time of a complete unit of time, it is possible in this example to achieve 75% of a complete electrophoresis, as shown in Fig. 5d. With the control means arranged to maintain the rectified voltage having superposed thereon the first alternating voltage for a predetermined length of time sufficient to be able to achieve a complete electrophoresis with the control means, and additionally arranged to cause the second alternating voltage, after a time shorter than the predetermined length of time, to make a phase jump of

substantially half a wavelength, a partial electrophoresis can be achieved in the predetermined length of time. In this way, therefore, it has become possible to control a desired extent of electrophoresis in a channel merely by jumping a phase as a function of the time. Of course, the extent of electrophoresis need not be proportional to the time in which the phase of the first and the second alternating voltage are opposite to each other. A non-proportional relation is also possible. Through calibration techniques, however, these relations can be easily determined by those skilled in the art.

It is of course also possible, instead of causing the phase to jump by half a wavelength, to cause the phase difference between the first and the second alternating voltage to become slightly more or slightly less than half a wavelength.

In a special structural variant, as shown in Fig. 6a and in Fig. 6b, the electrophoretic system included in a channel 1 is included in a matrix of multiple mutually separated channels 1 which are each provided with an electrophoretic system. Each channel 1 is provided, on a first side and on a second side, with a first electrode 2.y (y=1,2,3 ...) and a second electrode 3.x(x=1,2,3 ...), respectively. The matrix comprises at least two rows r.y (y=1,2,3 ...) and at least two columns k.x (x=1,2,3 ...). In each row r.y the first electrodes 2.y are electrically connected with each other, and in each column k.x the second electrodes 3.x are electrically connected with each other. Such a matrix may, for instance, be composed of a foil 4 provided with the channels 1. Each channel 1 is filled with an electrophoretic system comprising a medium having included therein electrically charged particles. In each row r.y the channels 1 may be closed on a first side with an electrode 2.y. In each column k.x the channels may be closed on a second side with a second electrode 3.x.

In this case, the device for controlling electrophoresis is therefore provided with multiple mutually separated channels 1 which are each

provided with an electrophoretic system. The channels 1 are further each provided, on a first side and on a second side situated substantially opposite the first side, with a first electrode and a second electrode, respectively. Furthermore, the channels are each included in a matrix, that is, arranged in a matrix comprising at least two rows and two columns. In each row the first electrodes are electrically connected with each other, and in each column the second electrodes are electrically connected with each other.

Hereinafter, the first electrode 2.y will be indicated as a row electrode 2.y, and the second electrode 3.x will be indicated as a column electrode 3.x.

With a method as will now be described, a predetermined desired extent of electrophoresis can be obtained in each channel 1 separately by imposing on the first electrode a voltage having a suitably selected voltage gradient and by imposing on the second electrode a suitably selected voltage gradient. In this example, the control of the electrophoresis is carried out per row. To this end, there is first selected a row in which the electrophoresis is to be controlled in each channel. In Fig. 6a there is imposed on the row electrode of the row r.1 a rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage. The voltage gradient of the voltage imposed on the row electrode 2.1 changes about a zero voltage, with a positive amplitude amounting to 3 V and a negative amplitude amounting to –4 V. When the electrophoretic system situated in the channel of row r.1 and column k.1 is not to change, then, as shown in Fig. 6a, to the second electrode, that is, the column electrode 3.1 of column k.1, a second alternating voltage generated in balance around a zero voltage will be applied. In this example, this alternating voltage has a positive amplitude of 3 V and a negative amplitude of –3 V. In effect, the voltage to which the electrophoretic system in the channel 1 positioned in row r.1 and column k.1 is subjected will have a gradient with alternately 0 V and –1 V. When in the electrophoretic system of the channel positioned in row r.1 and column k.3 an advanced

extent of electrophoresis is to take place, there is applied to the second electrode 3.3, the column electrode 3.3 of column k.3, a second alternating voltage generated in balance around a zero voltage. This second alternating voltage has a negative amplitude of –3 V and a positive amplitude of 3 V. Effectively, the electrophoretic system in the channel 1 positioned in row r.1 and column k.3 is subjected to a voltage gradient in which a positive amplitude of 6 V and a negative amplitude of –7 V alternate. As is known from the foregoing, an advanced extent of electrophoresis takes place in this channel 1. In this example, the alternating voltage applied to the column electrodes 3.1, 3.3 of column k.1 and column k.3 takes place in one unit of time. When in the electrophoretic system of the channel positioned in row r.1 and column k.2 an electrophoresis is to take place to an extent between the extent of electrophoresis of the channel 1 positioned in the row r.1 and column k.1 and the extent of electrophoresis of the channel 1 positioned in the row r.1 and column k.3, an alternating voltage can be applied to the second electrode 3.2, the column electrode 3.2 of column k.2, whereby after half a unit of time the alternating voltage makes a phase jump of half a wavelength. As can be seen in Fig. 6a, for instance for a first half unit of time, a second alternating voltage generated in balance around a zero voltage can be imposed on the column electrode of column k.2. The positive amplitude of this alternating voltage is 3 V, while the negative amplitude of this alternating voltage is –3 V. After half a unit of time, this alternating voltage can phase shift by half a wavelength. As is indicated with the represented numbers in the channel 1 positioned in row r.1 and column k.2, the electrophoretic system will in effect be subjected in the first half unit of time to a voltage having a voltage gradient in which a zero voltage is alternated by a voltage of –1 V, while in the second half unit of time the electrophoretic system is subjected to a voltage gradient in which 6 V and -7 V occur alternately. In the first half unit of time, electrophoresis will hardly, if at all, take place, while in the second half unit of time a far-

advanced extent of electrophoresis will take place. Since the time in which the far-advanced extent of electrophoresis will take place in the channel 1 positioned in row r.1 and column k.2 is half of the time in which a far-advanced extent of electrophoresis will take place in the channel positioned in row r.1 and column k.3, the far-advanced extent of electrophoresis will, in one unit of time, only partly take place in the channel 1 positioned in row r.1 and column k.2. It will be clear that the electrophoresis of the electrophoretic systems in all channels 1 positioned in row r.1 can be controlled simultaneously. It will also be clear that for the individual control of the electrophoresis in the electrophoretic systems positioned in row r.1 in one unit of time only the phase of an alternating voltage generated in balance around a zero voltage is used. In this example, the rectified voltage applied to the row electrode of row r.1 having superposed thereon the first alternating voltage is not changed in one unit of time. When the electrophoresis has been controlled to a desired extent in all the channels 1 positioned in row r.1, a zero voltage is applied to the first electrode 2.1 or the row electrode 2.1 of row r.1, as shown in Fig. 6b. Subsequently, a rectified voltage having superposed thereon an alternating voltage generated in balance around a zero voltage is applied to the row electrode 2.2 of the second row r.2.

When according to a predetermined program electrophoresis is hardly, if at all, to occur in the channel 1 positioned in row r.2 and column k.1, then, according to the predetermined program, in a second unit of time, a second alternating voltage generated in balance around a zero voltage is applied to the column electrode 3.1 of column k.1. This alternating voltage has a positive amplitude of 3 V and a negative amplitude of –3 V. The first alternating voltage imposed on the row electrode 2.1 and the second alternating voltage imposed on the column electrode 3.1 are in this case in phase with each other. Effectively, there is therefore generated over the electrophoretic system in the channel 1 positioned in row r.2 and column k.1

a voltage gradient in which a zero voltage is alternated with a voltage of -1 V. As known from the foregoing, hardly any electrophoresis will take place in the channel 1 positioned in row r.2 and column k.1 When according to the predetermined program a far-advanced extent of electrophoresis is to take place in the channel 1 positioned in row r.2 and column k.2, a second alternating voltage generated in balance around a zero voltage is applied to the column electrode 3.2 of column k.2. This second alternating voltage is opposite in phase to the phase of the alternating voltage applied to the row electrode 2.2. Therefore, as known from the foregoing, a far-advanced extent of electrophoresis will take place in the channel 1 positioned in row r.2 and column k.2. Subsequently, a partial electrophoresis can be controlled in the channel positioned in row r.2 and column k.3 in a manner similar to the control in the channel positioned in row r.1 and column k.2 , as shown in Fig. 6a. During the control of the electrophoresis of the channels positioned in row r.2, the second alternating voltage generated in balance around a zero voltage is applied to the column electrodes 3.1, 3.2, 3.3. Because a zero voltage is applied to the row electrode 2.1 of row r.1, the electrophoretic systems positioned in row r.1 are only subjected to the second alternating voltage generated in balance around a zero voltage. Since there is no rectified voltage component to which the electrophoretic systems positioned in row r.1, the already controlled electrophoresis in the systems positioned in row r.1 will not change. Similarly, the electrophoresis in each electrophoretic system positioned in a row can be controlled row by row. If it is known in advance to what extent electrophoresis is to take place in each individual electrophoretic system, a program can drive the row and column electrodes to subsequently control the desired extent of electrophoresis in each channel 1 in an efficient manner. When the devices shown in Figs. 6a and 6b are parts of electrophoretic displays, each electrophoretic system positioned in a channel 1 will comprise a display element. To obtain a desired image, it will be known in respect of each display element to which

extent electrophoresis is to take place in that display element. This information can be used when determining the program that drives the row and column electrodes. Of course, in a device according to Figs. 6a and 6b at least the row electrodes or the column electrodes are transparent when the device is used as part of a display. The starting position, or the position of the charged particles in the medium of each electrophoretic system, can be determined uniformly for all the electrophoretic systems in which the electrophoresis has not yet been controlled to the desired extent, by imposing a relatively higher rectified voltage to the row electrodes of the rows with electrophoretic systems whose electrophoresis has not been controlled yet. As a result, it is not necessary to, for instance, include in a display an extensive memory for fixing the starting position of a particular electrophoretic system, since this starting position will be determined by the previous image shown by the display. In Figs. 6a and 6b, a rectified voltage of 15 V is applied to the row electrodes 2.1, 2.2, 2.3 of the rows r.x with an electrophoretic system whose electrophoresis has not yet been controlled. The second alternating voltage of a relatively low amplitude, generated in balance about a zero voltage, applied to all column electrodes 3.1, 3.2, 3.3 will hardly influence the effect of the relatively high rectified voltage applied to the row electrode.

It will be clear that many variants of the device shown and the method described are possible. Smaller or greater phase differences may be used as well. It is also possible to provide the electrophoretic systems with oppositely charged particles. White particles that are, for instance, positively charged and black particles that are, for instance, negative charged may also be included in an electrophoretic system used as display element. It will also be clear that the amplitudes of the alternating voltage, as is shown in all the figures and in particular in Figs. 6a and 6b, may also be selected differently. The alternating voltages may also have forms that are different from the square-wave voltages shown in the figures. Those

skilled in the art will realize that the number of units of time and the number of wavelengths per unit of time can also be optimized for a selected electrophoretic system or selected multiple electrophoretic systems. It should further be clear that suitable amplitudes of the alternating voltages must be determined again for each electrophoretic system. Depending on the electrophoretic system, particular processes in an electrophoretic system can ensure that a wholly different set of amplitudes of the first alternating voltage and the second alternating voltage, and even the height of the rectified voltage, will achieve the effect as described in this application. Processes that can play a role in this regard may comprise the unraveling of parts that have coagulated, the generation and/or regeneration of charge and perhaps also the overcoming of a threshold voltage, for instance caused by the effect of sticking to the electrodes. For each electrophoretic system, however, the skilled person will be able to find a suitable first alternating voltage, second alternating voltage, rectified voltage, phase difference, and unit of time and form of the alternating voltage, to obtain the effect achieved with a method according to the invention. As stated, a device according to the invention is eminently suited for a display that may optionally be of flexible design by including the electrophoretic system in channels with which a foil is provided. These channels must then be covered using the row and column electrodes, while at least the column electrodes or the row electrodes are of transparent design.

As stated before, such a device is also suitable for use in a laboratory in which a controlled electrophoresis is to take place in a large number of electrophoretic systems. For instance in experiments on a large number of samples where in each sample an electrophoresis different from the electrophoresis of all other electrophoretic systems is to take place, a device and a method according to the invention can be used. In such a device and method, the voltage gradient imposed on the row electrodes need not be equal for each row. Thus, the amplitudes of the alternating voltage imposed

on each column electrode need not be equal either. In such a device and method, it is possible to carry out a huge number of electrophoresis experiments within a very short time. Such variants are each understood to fall within the scope of the invention.

5

CLAIMS

1. A device for controlling electrophoresis, which device is provided with an electrophoretic system included in a channel, comprising a multiplicity of charged particles included in a medium, which device is further provided with control means arranged to apply a rectified voltage across at least a part of the electrophoretic system, characterized in that the control means are further arranged to superpose on the rectified voltage an alternating voltage generated in balance around a zero voltage.

2. A device according to claim 1, characterized in that the channel is provided at a first channel end and at a second channel end with a first electrode and a second electrode, respectively, the control means being arranged to impose on the first electrode the rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage.

3. A device according to claim 2, characterized in that the control means are further arranged to impose on the second electrode a second alternating voltage generated in balance around a zero voltage.

4. A device according to claim 3, characterized in that the control means are further arranged to present the second alternating voltage in a phase substantially opposite to the phase of the first alternating voltage if according to a predetermined program the charged particles in the electrophoretic system are to change in position, and the control means are further arranged to present the second alternating voltage in a phase substantially equal to the phase of the first alternating voltage if according to the predetermined program the charged particles in the electrophoretic system are to substantially maintain an assumed position in the electrophoretic system.

5. A device according to claim 4, characterized in that the control means are arranged to maintain the rectified voltage with the first alternating voltage superposed thereon for a predetermined length of time, the control means further being arranged to cause, after a time shorter than the predetermined length of time, the second alternating voltage to make a phase jump of substantially half a wavelength to obtain a partial electrophoresis in the predetermined length of time.

6. A device according to any one of claims 1-5, characterized in that the electrophoretic system included in a channel is included in a matrix of mutually separate channels each provided with an electrophoretic system and each provided on a first and a second side with a first electrode and a second electrode, respectively, which matrix comprises at least two rows and at least two columns, while in each row the first electrodes are electrically connected with each other, and in each column the second electrodes are electrically connected with each other.

7. A device according to claim 6, characterized in that the control means are arranged to select, according to a predetermined sequence, a row for imposing on the first electrode of the selected row the rectified voltage with the first alternating voltage superposed thereon, and to control, according to the predetermined program, through imposing the second alternating voltage on each second electrode, a desired extent of electrophoresis in each electrophoretic system positioned in the selected row.

8. A device according to claim 7, characterized in that the control means are also arranged to impose on the first electrode of a row a zero voltage if the desired extent of electrophoresis has already been controlled in each electrophoretic system positioned in that row.

9. A device according to claim 7 or 8, characterized in that the control means are further arranged to impose a relatively high rectified voltage on the first electrode of a row of which in each electrophoretic system the desired extent of electrophoresis is yet to be controlled.

10. A device according to any one of the preceding claims, characterized in that the particles are provided with a color different from a color of the medium.

11. A device according to claim 10, characterized in that at least each first electrode or each second electrode is of transparent design.

12. A device according to any one of the preceding claims, characterized in that at least one of the particles comprises a biological substance.

13. A device according to claim 12, characterized in that at least one of the particles comprises at least a fragment of DNA.

14. A device according to claim 12 or 13, characterized in that at least one of the particles comprises a protein.

15. A device according to any one of the preceding claims, characterized in that the medium comprises a microporous gel.

16. A method for controlling electrophoresis of an electrophoretic system comprising a multiplicity of charged particles included in a medium, which method comprises:

- applying a rectified voltage across the electrophoretic system, characterized in that the method further comprises:
- applying across the electrophoretic system an alternating voltage generated in balance around a zero voltage, superposed on the rectified voltage.

17. A method according to claim 16, characterized in that the method comprises:

- imposing the rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage, on an electrode positioned on a first side of the system.

18. A method according to claim 17, characterized in that the method comprises:

- imposing a second alternating voltage generated in balance around a zero voltage on an electrode positioned on a second side of the system.

19. A method for controlling electrophoresis in multiple electrophoretic systems arranged in a matrix, each system at least comprising equally charged particles included in a medium, which matrix comprises at least two columns and at least two rows, the multiple electrophoretic systems being provided on a first side with row electrodes and on a second side with column electrodes, which method comprises:

- selecting a row of electrophoretic systems;
- imposing on the row electrode of the selected row a rectified voltage having superposed thereon a first alternating voltage generated in balance around a zero voltage;
- imposing on each column electrode a second alternating voltage generated in balance around a zero voltage.

20. A method according to claim 19, which method further comprises:

- selecting an electrophoretic system included in the selected row;
- arranging for the second alternating voltage to have a phase opposite to the phase of the first alternating voltage if according to a predetermined program the charged particles in the medium of the selected electrophoretic system are to change in position; and
- arranging for the second alternating voltage to have substantially a phase which is substantially equal to the phase of the first alternating voltage if according to a predetermined program the charged particles in the medium of the selected electrophoretic system are to substantially maintain an assumed position in the electrophoretic system.

21. A method according to claim 20, characterized in that the method comprises:

- maintaining for a predetermined length of time a rectified voltage with the first alternating voltage superposed thereon; and
- causing, after a time shorter than the predetermined length of time, the phase of the second alternating voltage to jump.

22. A method according to claim 21, characterized in that the method comprises:

- imposing a zero voltage to the first electrode of a row if a desired extent of electrophoresis has already been controlled in each electrophoretic system positioned in that row.

23. A method according to claim 21 or 22, characterized in that the method comprises:

- imposing a relatively high rectified voltage on the first electrode of a row of which in each electrophoretic system the desired extent of electrophoresis is yet to be controlled.

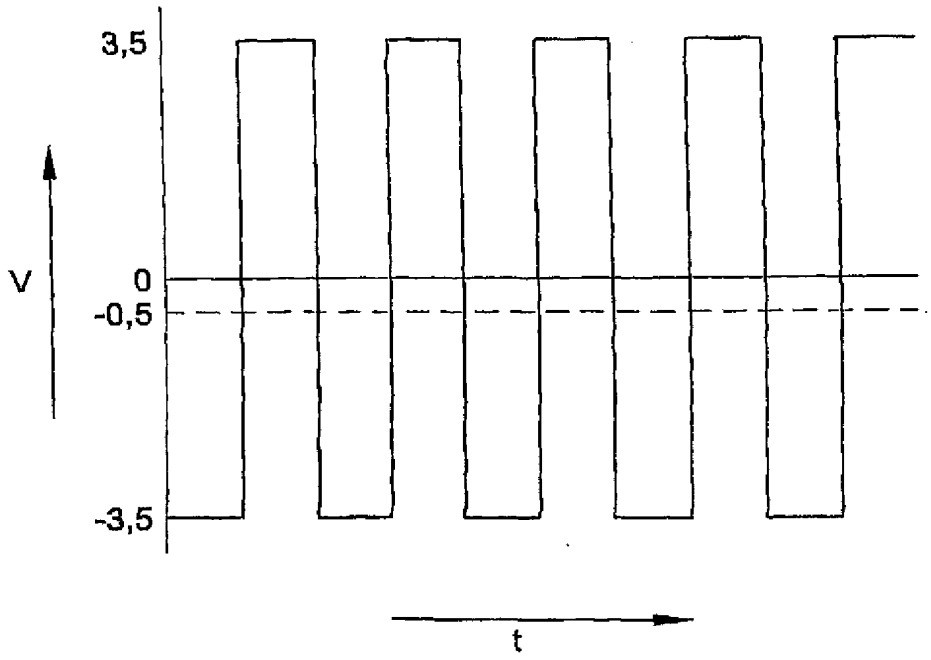

Fig. 1a

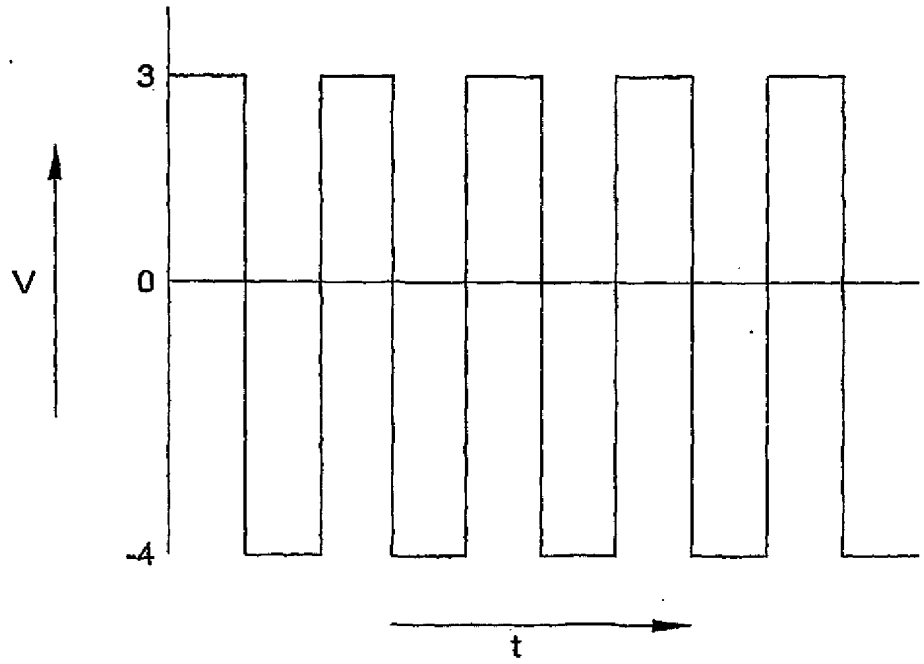

Fig. 1b

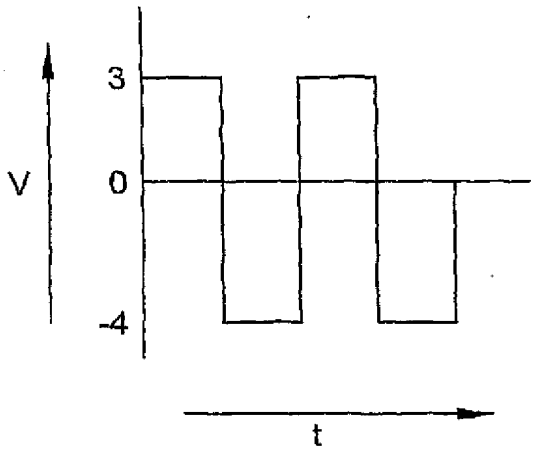

Fig. 2a

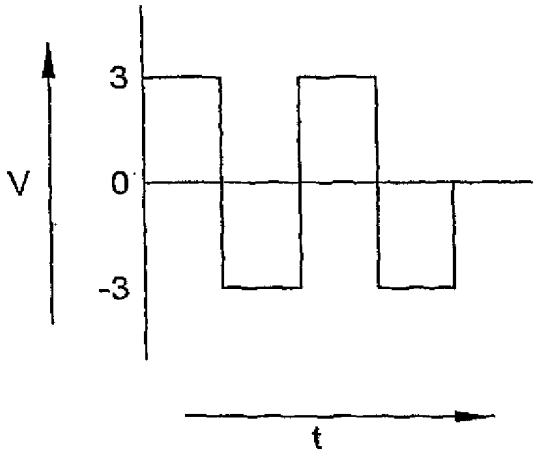

Fig. 2b

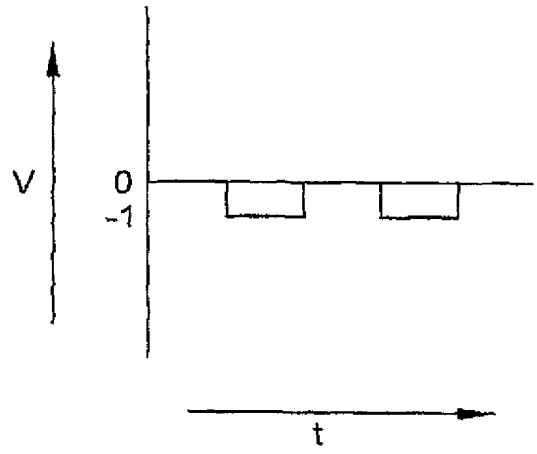

Fig. 2c

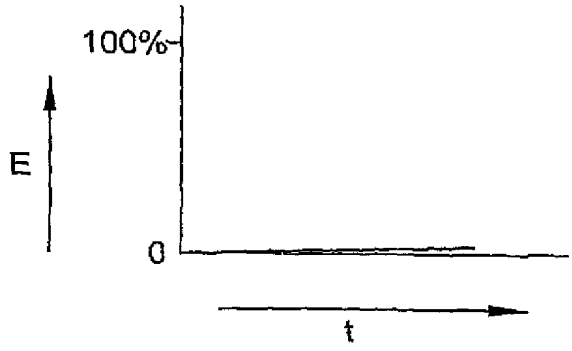

Fig. 2d

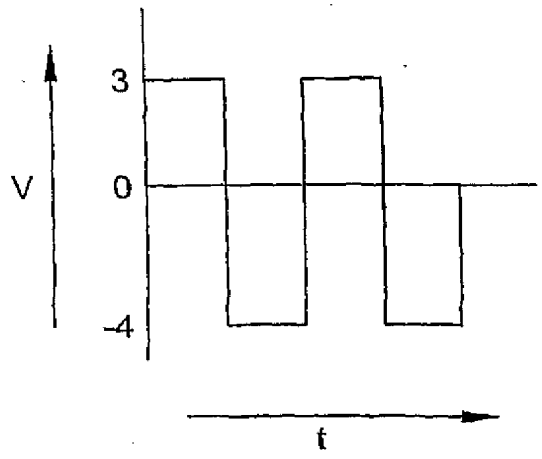

Fig. 3a

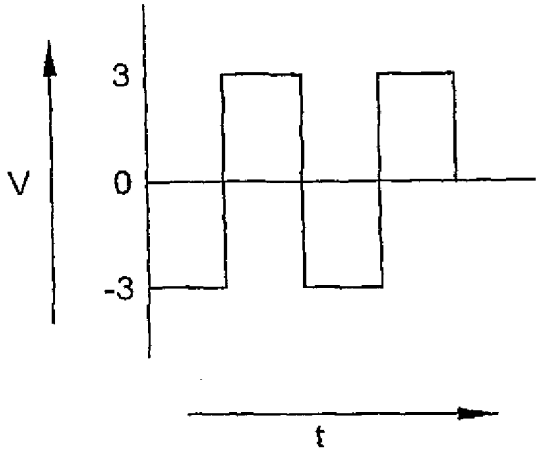

Fig. 3b

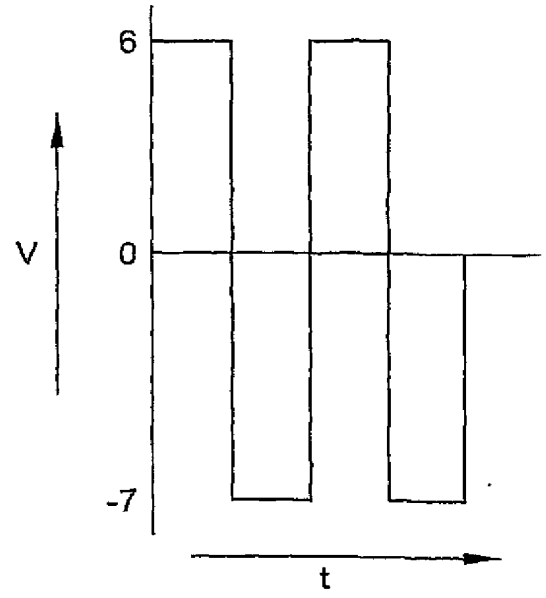

Fig. 3c

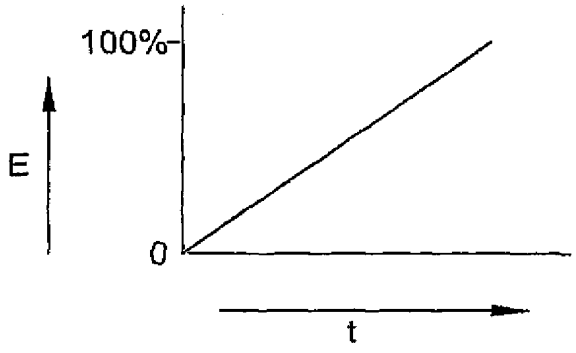

Fig. 3d

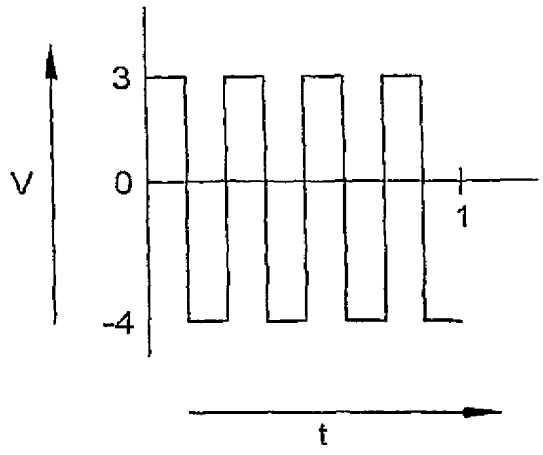

Fig. 4a

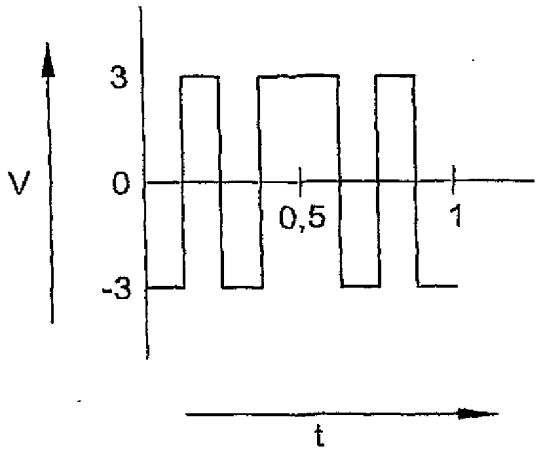

Fig. 4b

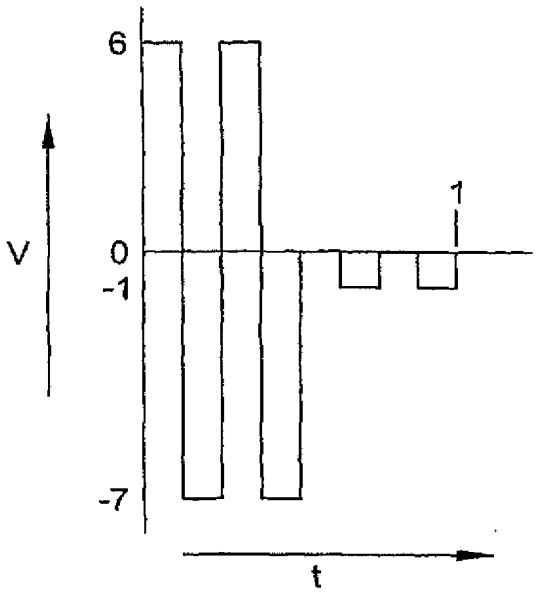

Fig. 4c

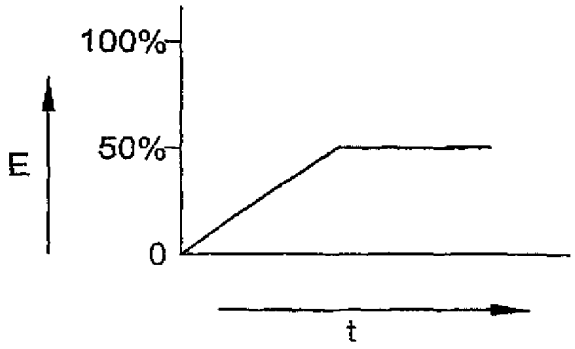

Fig. 4d

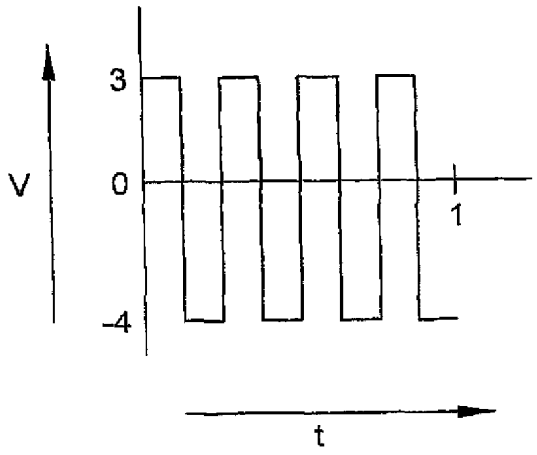

Fig. 5a

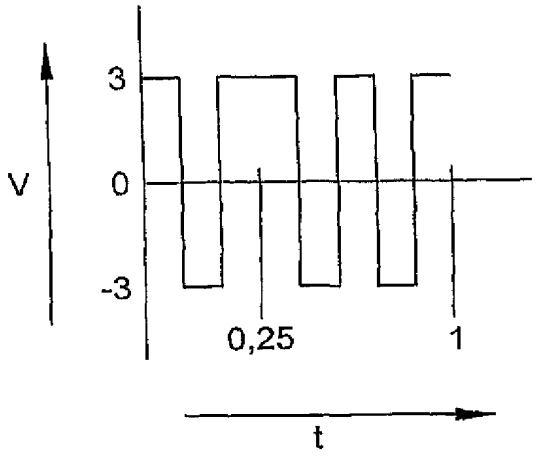

Fig. 5b

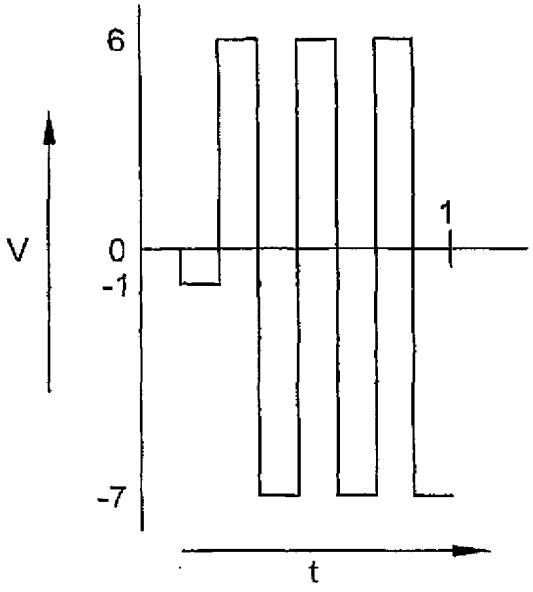

Fig. 5c

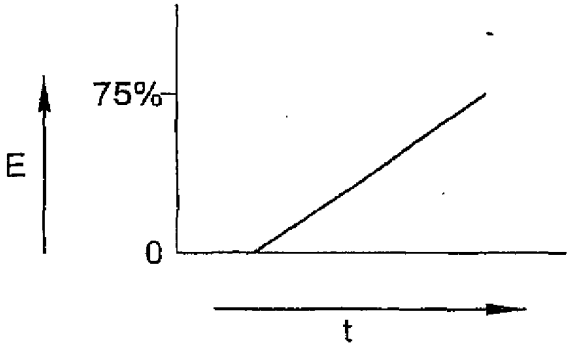

Fig. 5d

Fig. 6a

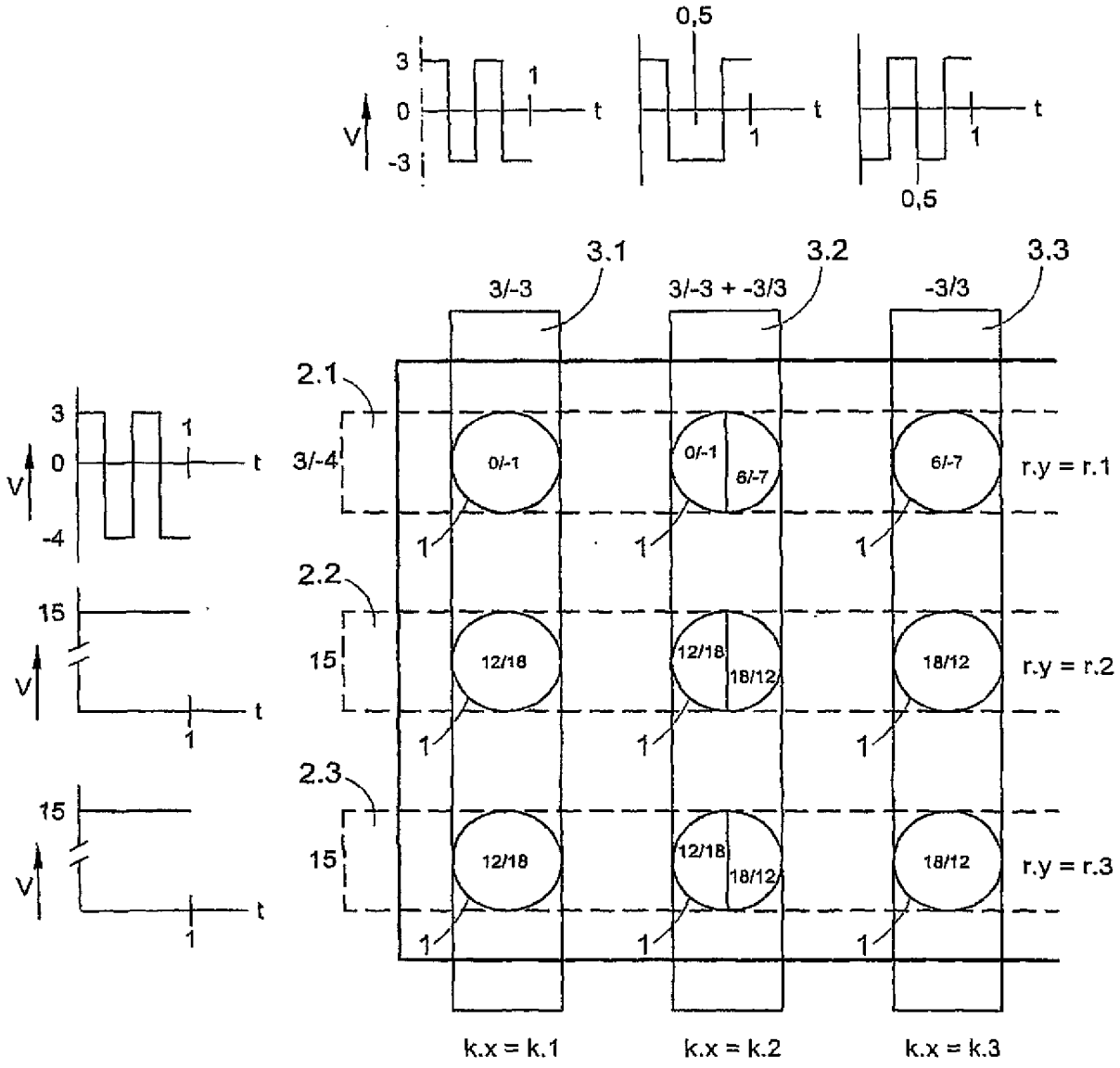
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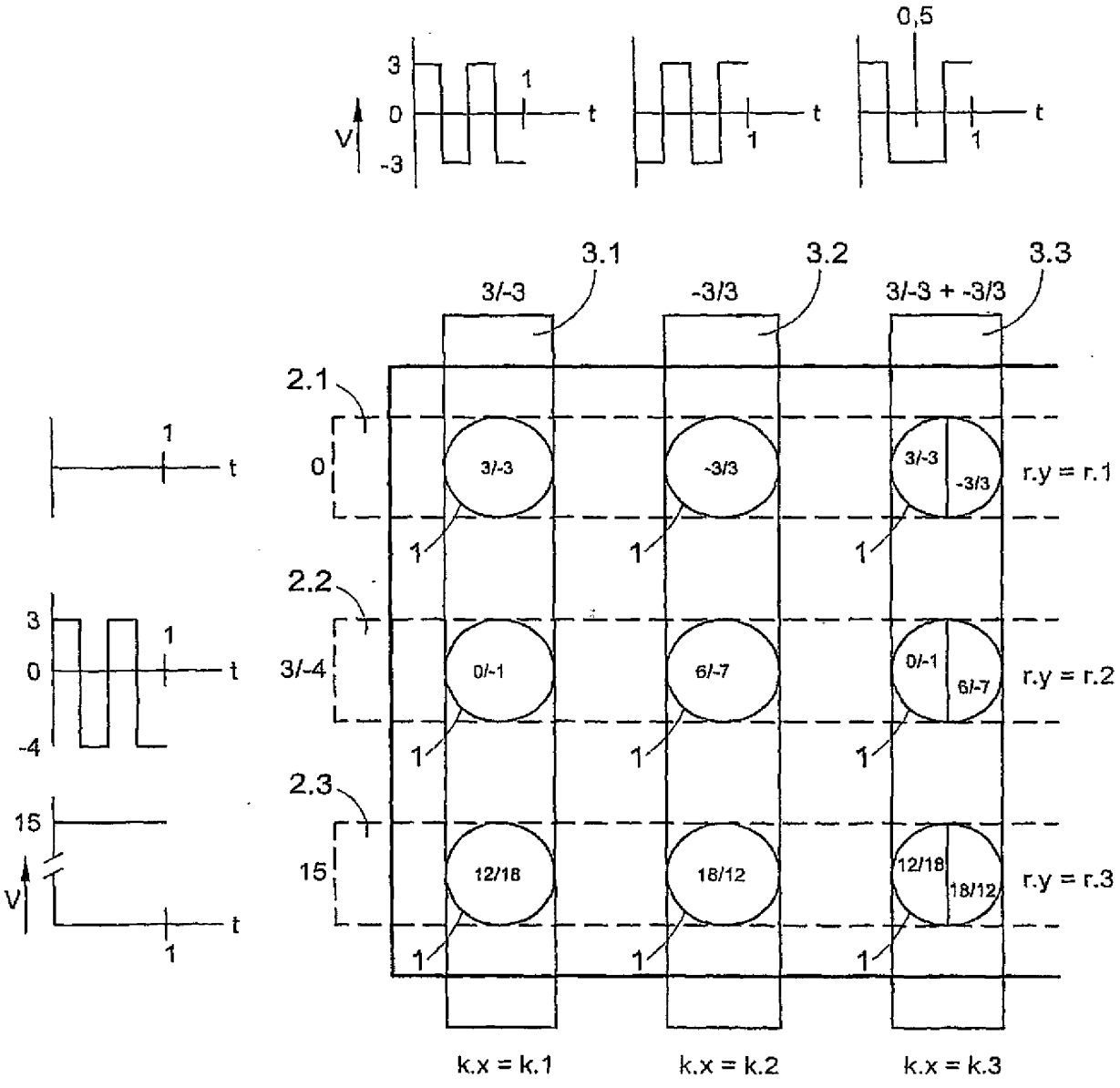
Fig. 6b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INTERNATIONAL SEARCH REPORT

Intern ation No
PCT/ [illegible] J0070

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G09G3/34 G02F1/167 G01N27/447

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G02F G09G G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, IBM-TDB, EPO-Internal, INSPEC, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 187 160 A (ZIMMERMANN ANDREAS) 5 February 1980 (1980-02-05) column 1, line 50 - line 65 column 2, line 32 - line 48; figure 1	1,16
A	US 4 041 481 A (SATO TERUO) 9 August 1977 (1977-08-09) column 3, line 44 -column 4, line 41 column 7, line 9 - line 39 column 9, line 3 - line 8; figures 1,7	1-11, 16-23
A	US 4 746 917 A (DI SANTO FRANK J ET AL) 24 May 1988 (1988-05-24) column 2, line 10 - line 52	1-10

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search	Date of mailing of the international search report
3 June 2003	13/06/2003

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Inter plication No
PCT/NL 03/00070

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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